12. (Twice Amended) A peptide consisting of an amino acid corresponding to amino acids 52 to 116 (SEQ ID No:9) of the sequence of the Rev protein of HIV-1 LAI isolate and containing T-cell epitopes within amino acids 63 to 73 (SEQ ID NO:3), 74 to 83 (SEQ ID NO:5) and 102 to 110 (SEQ ID NO:8)[, or consisting of a corresponding amino acid sequence from another HIV-I isolate].

REMARKS

This Continued Prosecution Application is submitted subsequent to the Final Action dated August 30, 1999.

The Examiner noted in the Final Action that neither the Amendment filed June 8, 1999, nor the Information Disclosure Statement filed June 29, 1999 contained a proper PTO-1449 and hence the references have not been considered. Our file shows a PTO-1449 to have accompanied the Amendment filed June 8, 1999 with copies of each of the documents cited therein, with the exception of USP 5,639,854 and EP 470,980. Copies of these references were indicated to be to follow and the documents received by the PTO on June 28, 1999 were those missing copies.

However, since it would appear that the PTO-1449 that accompanied the Amendment filed June 8, 1999 was mislaid in the Office, a further copy of the PTO-1449 is enclosed, along with copies of each of the references cited therein. Having regard thereto, it is requested that the references be considered.

The Examiner noted in the Final Action that the Oath or Declaration was defective and that a new Oath or Declaration identifying this application by its application number and filing date is required. The Examiner noted tat the Oath or Declaration is defective because:

1. it does not properly reference the specification as originally filed;
2. the signature of inventor Michel Klein is in the incorrect location and is undated.

In the Amendment filed June 8, 1999, the applicants noted an intention to file a new Declaration but the Examiner noted in the Final Action that no such document had been filed.

Submitted herewith is a new Declaration and Power of Attorney duly executed by all inventors and referring to this application by application number and filing date. It is submitted that the Declaration fully complies with 37 CFR 1.67(a).

The specific withdrawal of the rejection of claims 1 to 15 under 35 USC 103 in the Final Action is gratefully acknowledged.

In the Final Action, the Examiner maintained rejection of claims 2 to 4 and 6 to 15 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention.

With respect to claims 2 to 4, claims 2 and 3 have been deleted and claim 4 has been made dependent on claim 1.

With respect to claims 6 to 7, these claims have been amended to refer to amino acid sequences which are the same as those of a portion of an HIV-1 antigen. With respect to claim 12, the reference to a corresponding amino acid sequence from another HIV isolate has been deleted.

Having regard to the revisions made to the claims and the remarks contained herein, it is submitted that claims 2 to 4 and 6 to 15, insofar as they remain in the application and in their amended form, can no longer be considered indefinite and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner rejected claims 1 to 15 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invnetion.

The present invention is based on the findings that (1) two nanomer peptides, designated CLP-177 and CLP-72, a hexamer designated CLP-178 and a 12-mer designated CLP-182 of the HIV-1(LAI) REV protein were individually able to bind and stabilize membrane-bound the HLA class 1 molecule, HLA-A2;

and (2) that a long peptide (SEQ ID No: 9), encompassing the amino acid residues 52 to 116 of the HIV-1(LAI) Rev protein, and constructed by having a single cholesterol or palmitoyl moiety attached to its amino-(N-) terminus via a KSS linker to form lipopeptides, CLP-176 and CLP-175 respectively, are also capable of eliciting CTL as well as antibody responses in HLA-A2 transgenic mice.

Having regard to these experimental results, applicants have provided a sound immunization protocol for inducing a HIV-specific cytotoxic T-cell response in a host by initial administration of a T-helper molecule to prime the immune system of the host followed by administration of a mixture of the T-helper molecule and a T-cell epitope-containing peptide corresponding to a portion of an HIV antigen.

The invention is illustrated by using, as the T-helper molecule, peptides which correspond to a portion of the hepatitis B virus nucleocapsid antigen and, as the HIV T-cell epitope containing peptide, certain lipopeptides derived from the Rev protein, as discussed above. Clearly, however, the invention is applicable to other T-helper molecules and other HIV T-cell epitope containing peptides, and this is reflected in the language adopted in the claims.

In general, as recited in claim 1, applicants' invention is directed to a method of generating an HIV-specific cytotoxic T-cell response in a host. The procedure is a two-step operation, involving an initial administration of a T-helper molecule to provide T-helper cells of the immune system of the host and subsequently administering to the host a mixture of the T-helper molecule and a T-cell inducing HIV molecule to generate an HIV-specific CTL response in the host.

The Examiner noted in the Final Action that:

> "Applicants have not provided any convincing evidence that their claimed invention is indeed useful as a therapeutic or preventative for HIV infection . . ."

However, applicants' claims do not recite HIV infection therapy nor preventation of infection. Claim 1 recites only the generation of an HIV-specific cytotoxic T-cell response while claim 12 defines a specific peptide.

Having regard to the above, it is submitted that claims 1 to 15 fully comply with the provisions of 35 USC 112, first paragraph, and hence the rejection thereof should be withdrawn.

It is believed that this application now is in condition for allowance and early and favorable consideration and allowance are respectfully submitted.

Respectfully submitted,

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